PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 731217	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/AU2004/001480	International filing date *(day/month/year)* 27 October 2004	Priority date *(day/month/year)* 27 October 2003
International Patent Classification (IPC) or national classification and IPC Int. Cl. [7] C07K 2/00; A61K 38/19, 38/20, C07K 7/06, 14/715, 14/71; A61P 35/00, 43/00		
Applicant MEDVET SCIENCE PTY LTD et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
25 May 2005	13 October 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer KATHERINE MOERMAN Telephone No. (02) 6283 2714

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2004/001480

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1 (b))

   ☐ publication of the international application (under Rule 12.4)

   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

   ☒ the international application as originally filed/furnished

   ☐ the description:

   pages as originally filed/furnished
   pages* received by this Authority on with the letter of
   pages* received by this Authority on with the letter of

   ☐ the claims:

   pages as originally filed/furnished
   pages* as amended (together with any statement) under Article 19
   pages* received by this Authority on with the letter of
   pages* received by this Authority on with the letter of

   ☐ the drawings:

   pages as originally filed/furnished
   pages* received by this Authority on with the letter of
   pages* received by this Authority on with the letter of

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing (*specify*):
   ☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing (*specify*):
   ☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2004/001480

Box No. III **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos: **1-6 (in part)**

because:

☐ the said international application, or the said claims Nos.
relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos.
are so unclear that no meaningful opinion could be formed *(specify)*:

☒ the claims, or said claims Nos. **1-6 (in part)**
are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claim Nos. **1-6 (in part)**

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	14-60	YES
	Claims	1-13	NO
Inventive step (IS)	Claims		YES
	Claims	1-60	NO
Industrial applicability (IA)	Claims	1-60	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The following documents, cited in the ISR, were considered for the purposes of this report:

D1 DATABASE NCBI (protein) Accession Number: AAA18171, 16 May 1994

D2 Bone H. and Welham M. J., Cellular Signalling, 2000, volume 12, pages 183-194

D3 Stomski F. C. et al., Blood, 1999, volume 94 (number 6), pages 1933-1942

D4 Guthridge M. A. et al., Stem Cells, 1998, volume 16 pages 301-313

D5 Itoh T. et al., The Journal of Biological Chemistry, 1996, volume 271 (number 13), pages 7587-7592

The invention of the present application is directed to the identification of a binding motif which contains the sequence NXXY. Claims 1-13 are directed to the binding motif. Claims 14-42 and 51-53 are directed to methods of modulating cellular activity. Claims 43-49 are directed to methods relating to the transplantation of cells. Claims 50, 52 and 53 are directed to methods for improving wound healing. Claims 54-57 and 60 are directed to the use of a substance which inhibits the activation of a tyrosine in a binding motif for the preparation of a medicament. Claims 58 and 59 are directed to methods for screening cell growth promoting compounds. While comments have been made regarding the dependency of some of the claims (Box VII), for the purposes of this opinion they have been considered as outlined above.

Claims 1-9, 12 and 13 are *prima facie* not novel in the light of the admitted prior art. Any protein, or peptide with the sequence NXXY is considered to anticipate claims to the binding motif (Box VIII). The sequences defined in Claim 4 are derived from known proteins (pages 12, 13). Consequently these proteins anticipate the claims.

D1 discloses the amino acid sequence of the common β chain of the GM-CSF, IL-3 and IL-5 receptors. Given that any protein, polypeptide or peptide with the sequence NXXY is considered to anticipate claims to the binding motif (Box VIII) Claims 1-13 are not novel in the light of D1. D1 does not disclose any information regarding methods of use of the protein. Therefore, Claims 14-60 are considered novel and inventive in the light of D1.

D2 discloses that the PTB domain of Shc interacts with the β chain at tyr577 and that NGPY is the binding sequence (section 3.6, 3.7 and discussion). Shc is known to be involved in the IL-3 signalling pathway and therefore, effects the cellular survival and proliferation. The mutation of tyr577 to phenylalanine, which results in the abolition of Shc activation is discussed in D2. D2 anticipates Claims 1-13 of the present application. D2 does not explicitly state the consequences of identifying the binding motif of Shc with the β chain. However, given that the signalling pathways and influence of IL-3 are known it would be obvious to the person skilled in the art that the manipulation of such signalling would result in the alteration of cellular activity as defined in the present claims. Therefore, Claims 14-60 lack an inventive step in the light of D2

Continued in supplemental box

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

a) Claims 1-6 are not fully supported by the description with respect to the term "binding motif". Independent Claims 1 and 2 define a binding motif capable of binding to a cytosolic protein and having the sequence NXXY.

Firstly, the use of the term "capable" indicates that the ability of the binding motif to bind to a cytosolic protein is not a limiting feature of the claim.

Secondly, protein-protein interactions depend not only on sequence (primary structure) but also secondary, tertiary and quaternary protein structure. Therefore, it appears that the claim is not directed to the four amino acids 'NXXY' in isolation but includes within its scope any protein or peptide that includes the sequence NXXY within its primary structure. The ability of one protein to bind to another protein is a property which is inherent to the proteins. Identifying and specifying the mechanism by which certain proteins interact does not render a claim to the proteins novel. Consequently, any protein or peptide which contains the sequence NXXY is considered to be highly relevant to the claims of the present application.

Thirdly, the description provides support only for the interaction of the motif found in the common β chain of the GM-CSF, IL-3 and IL-5 receptors at residues 574-577.

Therefore, Claims 1-6 are considered to lack the support of the description.

b) Claim 4 is not clear in scope or fully supported with respect to the phase "binding motif or equivalent thereof". There is no indication what an equivalent of the binding motif is within the claim. Furthermore, the definition provided within the description at page 11 for "functional equivalent or analogue thereof" is not clear in scope or fully supported as it defines potential equivalent proteins by the activity and function.

c) Claim 22 appears to be incorrectly appended to Claim 23. Claim 23 is directed to decreasing the phosphorylation of the Tyr by subjecting the cell to an antagonist, that is, indirect modification of the Tyr residue. Claim 22, which is appended to Claim 23 is directed to the direct modification of the binding motif by substituting the Tyr residue for Phe. It is perhaps more appropriate for Claim 22 to be appended to Claim 21 which is also directed to the direct modification of the binding motif.

d) Claims 38 and 39 appear to be incorrectly appended. These claims are dependent on Claims 34 and 35 respectively which in turn are appended to independent claims 14 and 15. The features defined in Claims 38 are also defined in Claim 16. The features defined in Claim 39 are also defined in Claim 17. Consequently, Claims 38 and 39 are redundant. However, Claims 38 and 39 follow independent Claim 37. The features defined in Claims 38 and 39 are not defined in the claims which are associated with independent Claim 37. Therefore, it seems more appropriate for Claims 38 and 39 to be appended to independent Claim 37.

Similarly, Claim 60 as appended to Claim 56 but follows independent Claim 58. The features defined in Claim 60 are also defined in Claim 57 resulting in Claim 60 being redundant. Therefore, it seems more appropriate for Claim 60 to be appended to Claim 58.

e) Claim 53 is redundant as the features which it defines are already defined in Claim 52 to which it is appended.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: V

D3 discloses a motif involving tyr577. Specifically, D3 discloses that the adaptor protein 14-3-3 ζ binds to residues 582-587 of the common β chain of the GN-CSF, IL-3 and IL-5 receptors. It is suggested that the proximity of tyr577 to the 14-3-3 binding site forms a distinct motif which is involved in specialized functions for the associated receptors (see discussion, paragraph 1). However, D3 does not disclose or suggest that the motif NXXY is capable of binding to a cytoplasmic protein and the amino acid residues upstream of tyr577 are not considered with respect to the motif disclosed. Therefore, Claims 1-60 are considered novel and inventive in the light of D3.

D4 discloses that the survival domain 'box 3' of the β chain (amino acid residues 570-626) is involved in signalling. D4 states "What motifs within this conserved domain are responsible for signalling, and how do they signal? Although this question addresses one of the most fundamental aspects of GM-CSF biology, the answer has remained elusive." (page 308, right column, first paragraph). D4 acknowledges the interaction between SHC and grb2 proteins with tyr577. However, D4 does not disclose or suggest that the motif NXXY is capable of binding to a cytoplasmic protein and the amino acid residues surrounding tyr577 are not considered in relation to protein binding. Therefore, Claims 1-60 are considered novel and inventive in the light of D4.

D5 discloses that Tyr577 is critical for the activation of Shc and mediates PTP1D phosphorylation. However, D5 does not disclose or suggest that the motif NXXY is capable of binding to a cytoplasmic protein and the amino acid residues surrounding tyr577 are not considered in relation to protein binding. Therefore, Claims 1-60 are considered novel and inventive in the light of D5.

The subject matter defined in the claims is considered to be industrially applicable.